## AUG 2 5 ZOOK NO

## SEQUENCE LISTING

<110> Hammock, Bruce D.

Kim, In-Hae

Morisseau, Christophe

Watanabe, Takaho

Newman, John W.

The Regents of the University of California

- <120> Improved Inhibitors for the Soluble Epoxide Hydrolase
- <130> 02307W-131010US
- <140> US 10/817,334
- <141> 2004-04-02
- <150> US 60/460,559
- <151> 2003-04-03
- <160> 4
- <170> PatentIn Ver. 2.1
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- <211> 555
- <212> PRT
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- <220>
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- Ala Thr Thr Arg Leu Met Lys Gly Glu Ile Thr Leu Ser Gln Trp Ile
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- Arg Lys Cly Phe Thr Thr Ala Ile Leu Thr Asn Thr Trp Leu Asp 115 120 125
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Pro Thr Glu Gln Leu Met Lys Gly Lys Ile Thr Phe Ser Gln Trp Val
50 55 60

Pro Leu Met Asp Glu Ser Cys Arg Lys Ser Ser Lys Ala Cys Gly Ala 65 70 75 80

Ser Leu Pro Glu Asn Phe Ser Ile Ser Glu Ile Phe Ser Gln Ala Met 85 90 95

Ala Ala Arg Ser Ile Asn Arg Pro Met Leu Gln Ala Ala Ala Leu 100 105 110

Lys Lys Gly Phe Thr Thr Cys Ile Val Thr Asn Asn Trp Leu Asp 115 120 125

Asp Ser Asp Lys Arg Asp Ile Leu Ala Gln Met Met Cys Glu Leu Ser 130 135 140

Gln His Phe Asp Phe Leu Ile Glu Ser Cys Gln Val Gly Met Ile Lys 145 150 155 160

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165 170 175

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Leu Lys Arg Gly His Ile Glu Asp Cys Gly His Trp Thr Gln Ile Glu 515 520 525

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Ile Gln Asn Pro Ser Val Thr Ser Lys Ile 545 550

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<213> Mus musculus

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Pro Thr Glu Gln Leu Met Lys Gly Lys Ile Thr Phe Ser Gln Trp Val 50 55 60

Pro Leu Met Asp Glu Ser Tyr Arg Lys Ser Ser Lys Ala Cys Gly Ala 65 70 75 80

Asn Leu Pro Glu Asn Phe Ser Ile Ser Gln Ile Phe Ser Gln Ala Met 85 90 95

Ala Ala Arg Ser Ile Asn Arg Pro Met Leu Gln Ala Ala Ile Ala Leu 100 105 110

Lys Lys Gly Phe Thr Thr Cys Ile Val Thr Asn Asn Trp Leu Asp 115 120 125

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Pro Glu Pro Gln Ile Tyr Asn Phe Leu Leu Asp Thr Leu Lys Ala Lys 165 170 175

Pro Asn Glu Val Val Phe Leu Asp Asp Phe Gly Ser Asn Leu Lys Pro 180 185 190

Ala Arg Asp Met Gly Met Val Thr Ile Leu Val His Asn Thr Ala Ser

Ala Leu Arg Glu Leu Glu Lys Val Thr Gly Thr Gln Phe Pro Glu Ala 210 215 220

Pro Leu Pro Val Pro Cys Asn Pro Asn Asp Val Ser His Gly Tyr Val 230 235 Thr Val Lys Pro Gly Ile Arg Leu His Phe Val Glu Met Gly Ser Gly Pro Ala Leu Cys Leu Cys His Gly Phe Pro Glu Ser Trp Phe Ser Trp Arg Tyr Gln Ile Pro Ala Leu Ala Gln Ala Gly Phe Arg Val Leu Ala Ile Asp Met Lys Gly Tyr Gly Asp Ser Ser Pro Pro Glu Ile Glu Glu Tyr Ala Met Glu Leu Leu Cys Lys Glu Met Val Thr Phe Leu Asp 310 315 Lys Leu Gly Ile Pro Gln Ala Val Phe Ile Gly His Asp Trp Ala Gly Val Met Val Trp Asn Met Ala Leu Phe Tyr Pro Glu Arg Val Arg Ala Val Ala Ser Leu Asn Thr Pro Phe Met Pro Pro Asp Pro Asp Val Ser Pro Met Lys Val Ile Arg Ser Ile Pro Val Phe Asn Tyr Gln Leu Tyr Phe Gln Glu Pro Gly Val Ala Glu Ala Glu Leu Glu Lys Asn Met Ser 390 Arg Thr Phe Lys Ser Phe Phe Arg Ala Ser Asp Glu Thr Gly Phe Ile 410 Ala Val His Lys Ala Thr Glu Ile Gly Gly Ile Leu Val Asn Thr Pro Glu Asp Pro Asn Leu Ser Lys Ile Thr Thr Glu Glu Glu Ile Glu Phe 440 Tyr Ile Gln Gln Phe Lys Lys Thr Gly Phe Arg Gly Pro Leu Asn Trp 460 Tyr Arg Asn Thr Glu Arg Asn Trp Lys Trp Ser Cys Lys Gly Leu Gly Arg Lys Ile Leu Val Pro Ala Leu Met Val Thr Ala Glu Lys Asp Ile Val Leu Arg Pro Glu Met Ser Lys Asn Met Glu Lys Trp Ile Pro Phe Leu Lys Arg Gly His Ile Glu Asp Cys Gly His Trp Thr Gln Ile Glu

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Val Gln Asn Pro Ser Val Thr Ser Lys Ile 545 550

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<213> Mus musculus

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Met Asp Glu Ser Tyr Arg Lys Ser Ser Lys Ala Cys Gly Ala Asn Leu
50 55 60

Pro Glu Asn Phe Ser Ile Ser Gln Ile Phe Ser Gln Ala Met Ala Ala 65 70 75 80

Arg Ser Ile Asn Arg Pro Met Leu Gln Ala Ala Ile Ala Leu Lys Lys 85 90 95

Lys Gly Phe Thr Thr Cys Ile Val Thr Asn Asn Trp Leu Asp Asp Gly
100 105 110

Asp Lys Arg Asp Ser Leu Ala Gln Met Met Cys Glu Leu Ser Gln His
115 120 125

Phe Asp Phe Leu Ile Glu Ser Cys Gln Val Gly Met Ile Lys Pro Glu 130 135 140

Pro Gln Ile Tyr Asn Phe Leu Leu Asp Thr Leu Lys Ala Lys Pro Asn 145 150 155 160

Glu Val Val Phe Leu Asp Asp Phe Gly Ser Asn Leu Lys Pro Ala Arg 165 170 175

Asp Met Gly Met Val Thr Ile Leu Val His Asn Thr Ala Ser Ala Leu 180 185 190

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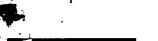
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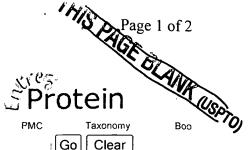


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Entrez

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Nucleotide

Protein

Genome

Structure

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Feat

☐ **1:** <u>P80299</u>. Soluble epoxide h...[gi:462371]

Limits

BLink, Domains, Links

LOCUS

P80299

554 aa

linear

ROD 15-JUN-2004

DEFINITION

Soluble epoxide hydrolase (SEH) (Epoxide hydratase) (Cytosolic epoxide hydrolase) (CEH).

ACCESSION

P80299

P80299 GI:462371

VERSION DBSOURCE

swissprot: locus HYES\_RAT, accession P80299;

class: standard. created: Feb 1, 1994.

sequence updated: Feb 1, 1994. annotation updated: Jun 15, 2004.

xrefs: gi: 402631, gi: 402632, gi: 55929, gi: 55930, gi: 477003
xrefs (non-sequence databases): HSSPP34914, MEROPSS33.973,

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PRINTSPR00412, PRINTSPR00413, TIGRFAMsTIGR01509

KEYWORDS Hydrolase; Peroxisome; Detoxification; Aromatic hydrocarbons

catabolism; Direct protein sequencing.

SOURCE

Rattus norvegicus (Norway rat)

ORGANISM Rattus norvegicus

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae;

Rattus.

REFERENCE 1 (residues 1 to 554)

AUTHORS Knehr, M., Thomas, H., Arand, M., Gebel, T., Zeller, H.D. and Oesch, F.

TITLE Isolation and characterization of a cDNA encoding rat liver cytosolic epoxide hydrolase and its functional expression in

Escherichia coli

JOURNAL J. Biol. Chem. 268 (23), 17623-17627 (1993)

MEDLINE <u>93352557</u> PUBMED 8349641

REMARK SEQUENCE FROM N.A.

STRAIN=Sprague-Dawley; TISSUE=Liver

REFERENCE 2 (residues 1 to 554)

AUTHORS Arand, M., Knehr, M., Thomas, H., Zeller, H.D. and Oesch, F.

TITLE An impaired peroxisomal targeting sequence leading to an unusual bicompartmental distribution of cytosolic epoxide hydrolase

FEBS Lett. 294 (1-2), 19-22 (1991)

MEDLINE 92077134 PUBMED 1743286

REMARK SEQUENCE OF 450-554 FROM N.A., AND PARTIAL SEQUENCE.

TISSUE=Liver

COMMENT

**JOURNAL** 

This SWISS-PROT entry is copyright. It is produced through a collaboration between the Swiss Institute of Bioinformatics and the EMBL outstation - the European Bioinformatics Institute. The original entry is available from http://www.expasy.ch/sprot

and <a href="http://www.ebi.ac.uk/sprot">http://www.ebi.ac.uk/sprot</a>

\_\_\_\_\_\_

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[FUNCTION] This enzyme acts on epoxides (alkene oxides, oxiranes)
            and arene oxides. Plays a role in xenobiotic metabolism by
            degrading potential toxic epoxides. Also determines steady-state
            levels of physiological mediators.
            [CATALYTIC ACTIVITY] An epoxide + H(2)O = a glycol.
            [SUBUNIT] Homodimer.
            [SUBCELLULAR LOCATION] Cytoplasmic and peroxisomal.
            [INDUCTION] By compounds that cause peroxisome proliferation such
            as clofibrate, tiadenol and fenofibrate.
            [SIMILARITY] Belongs to the AB hydrolase superfamily. Epoxide
            hydrolase family.
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11
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Nucleotide

Genome

Structure

PMC Go

Limits

default Show: 20

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Protein

History File

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☐ 1: JC4711. epoxide hydrolase...[gi:2135082]

BLink, Domains, Links

LOCUS JC4711 555 aa linear PRI 17-MAR-2000

epoxide hydrolase (EC 3.3.2.3) 2, cytosolic - human. DEFINITION

JC4711 ACCESSION

VERSION JC4711 GI:2135082 **DBSOURCE** pir: locus JC4711;

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genetic: #gene GDB:EPHX2 ##cross-references GDB:371845; OMIM:132811 #map position 8p21-8p12 #introns 34/2; 62/3; 116/1; 179/3; 220/3; 245/3; 277/3; 304/1; 315/3; 324/3; 353/2; 390/3; 414/3; 426/1;

460/3; 483/3; 510/3; 530/ 2

PIR dates: 16-Aug-1996 #sequence revision 16-Aug-1996 #text change

17-Mar-2000

**KEYWORDS** aromatic hydrocarbon catabolism; detoxification; ether hydrolase;

liver.

Homo sapiens (human) SOURCE

ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

(residues 1 to 555) REFERENCE

**AUTHORS** Beetham, J.K., Tian, T. and Hammock, B.D.

TITLE cDNA cloning and expression of a soluble epoxide hydrolase from

human liver

Arch. Biochem. Biophys. 305 (1), 197-201 (1993) **JOURNAL** 

MEDLINE 93343630 8342951 PUBMED

(residues 1 to 555) REFERENCE **AUTHORS** Sandberg, M. and Meijer, J.

Structural characterization of the human soluble epoxide hydrolase TITLE

gene (EPHX2)

**JOURNAL** Biochem. Biophys. Res. Commun. 221 (2), 333-339 (1996)

MEDLINE 96192049 **PUBMED** 8619856

This enzyme is involved in the conversion of harmful COMMENT

epoxide-containing compounds into diols.

Location/Qualifiers **FEATURES** 

> 1..555 source

> > /organism="Homo sapiens" /db xref="taxon:9606"

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/product="epoxide hydrolase 2, cytosolic"

/EC number="3.3.2.3"

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